WEST Search History

DATE: Wednesday, May 28, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L5	L4 and (micronize or micronized or particle or microparticles or microsohere or microcapsule)	7	L5
L4	(l2 or L3) and drospirenone	17	L4
L3	(oral) same (hormone adj replacement adj therapy) and (estrogen adj10 (progestogen or preogesterone or levonorgestrol or norethisterone))	13	L3
L2	(oral or tablet or pill or capsule) same (hormone adj replacement adj therapy or estrogen adj10 progestogen)	265	L2
L1	drospirenone same spironolactone	0	L1

END OF SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 18:40:54 ON 28 MAY 2003)

FILE 'CAPLUS' ENTERED AT 18:41:32 ON 28 MAY 2003

L1 1051139 SEA ABB=ON PLU=ON (MICRONIZE OR MICROPARTICLE OR MICRONIZED OR PARTICULATE OR MICROSPHERE OR MICROCAPSULE OR PARTICLE)

L2 156 SEA ABB=ON PLU=ON L1 (P) (PROGESTOGEN OR DROSPIRENONE OR PROGESTIN OR NORETHISTERONE OR LEVO-NORGESTREL OR CYPROTERONE OR CHLORMADIONE OR NORGESTREL OR KETODESOGESTREL)

L3 87 SEA ABB=ON PLU=ON L1 (P) (DROSPIRENONE OR PROGESTOGEN OR PROGESTIN)

L4 37 SEA ABB=ON PLU=ON L1 (P) (DROSPIRENONE OR PROGESTOGEN)

L5 4 SEA ABB=ON PLU=ON L1 (P) (DROSPIRENONE)

L6 33 SEA ABB=ON PLU=ON L1 (P) (PROGESTOGEN)

L7 12 SEA ABB=ON PLU=ON (L6 OR L5 OR L4 OR L3 OR L2) (P) (BIOAVAILABILITY OR DSISSOLUTION OR ABSORPTION OR AVAILABILITY OR PLASMA (2A) CONCNETRATION)

D L7 IBIB KWIC 1-

D L5 IBIB KWIC 1-

L8 4 SEA ABB=ON PLU=ON (L6 OR L5) (P) (BIOAVAILABILITY OR DSISSOLUTION OR ABSORPTION OR AVAILABILITY OR PLASMA (2A) CONCNETRATION)

D L8 IBIB KWIC 1-

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     (FILE 'HOME' ENTERED AT 18:40:54 ON 28 MAY 2003)

     FILE 'CAPLUS' ENTERED AT 18:41:32 ON 28 MAY 2003
L1      1051139 SEA ABB=ON  PLU=ON  (MICRONIZE OR MICROPARTICLE OR MICRONIZED
                OR PARTICULATE OR MICROSPHERE OR MICROCAPSULE OR PARTICLE)
L2          156 SEA ABB=ON  PLU=ON  L1 (P) (PROGESTOGEN OR DROSPIRENONE OR
                PROGESTIN OR NORETHISTERONE OR LEVO-NORGESTREL OR CYPROTERONE
                OR CHLORMADIONE OR NORGESTREL OR KETODESOGESTREL)
L3           87 SEA ABB=ON  PLU=ON  L1 (P) (DROSPIRENONE OR PROGESTOGEN OR
                PROGESTIN)
L4           37 SEA ABB=ON  PLU=ON  L1 (P) (DROSPIRENONE OR PROGESTOGEN)
L5            4 SEA ABB=ON  PLU=ON  L1 (P) (DROSPIRENONE)
L6           33 SEA ABB=ON  PLU=ON  L1 (P) (PROGESTOGEN)
L7           12 SEA ABB=ON  PLU=ON  (L6 OR L5 OR L4 OR L3 OR L2) (P) (BIOAVAILA
                BILITY OR DSISSOLUTION OR ABSORPTION OR AVAILABILITY OR PLASMA
                (2A) CONCNETRATION)
                D L7 IBIB KWIC 1-
                D L5 IBIB KWIC 1-
L8            4 SEA ABB=ON  PLU=ON  (L6 OR L5) (P) (BIOAVAILABILITY OR
                DSISSOLUTION OR ABSORPTION OR AVAILABILITY OR PLASMA (2A)
                CONCNETRATION)
                D L8 IBIB KWIC 1-

     FILE 'REGISTRY' ENTERED AT 18:57:22 ON 28 MAY 2003
                E DROSPIRENONE/CN
                E E3
L9            1 SEA ABB=ON  PLU=ON  DROSPIRENONE/CN
                D E3
                D L9

     FILE 'CAPLUS' ENTERED AT 19:00:20 ON 28 MAY 2003
                S 67392-87-4/REG#

     FILE 'REGISTRY' ENTERED AT 19:00:40 ON 28 MAY 2003
L10           1 SEA ABB=ON  PLU=ON  67392-87-4/RN

     FILE 'CAPLUS' ENTERED AT 19:00:40 ON 28 MAY 2003
L11          99 SEA ABB=ON  PLU=ON  L10

     FILE 'CAPLUS' ENTERED AT 19:00:49 ON 28 MAY 2003
L12          13 SEA ABB=ON  PLU=ON  1,2-DIHYDROSPIRORENONE OR DIHYDROSPIRORENON
                E OR 3-OXO-6.BETA.,7.BETA.:15.BETA.,16.BETA.-DIMETHYLENE-17.ALP
                HA.-PREGN-4-EN-21,17-CARBOLACTONE
L13           0 SEA ABB=ON  PLU=ON  L12 (P) (MICRONIZED OR MICROPARTICLES OR
                PARTICLE OR MICROSPHERE OR MICROCAPSULE)
L14           0 SEA ABB=ON  PLU=ON  L12 AND (MICRONIZED OR MICROPARTICLES OR
                PARTICLE OR MICROSPHERE OR MICROCAPSULE)
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4 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:174853 CAPLUS
DOCUMENT NUMBER: 130:262341
TITLE: Oral micronized progesterone
AUTHOR(S): De Lignieres, Bruno
CORPORATE SOURCE: Department of Endocrinology and Reproductive Medicine, Hopital Necker, Paris, Fr.
SOURCE: Clinical Therapeutics (1999), 21(1), 41-60
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB This review sought to examine the rationale for selecting an oral **micronized** progesterone formulation rather than a synthetic **progestin** for some of the main indications for progestogens. Unopposed **estrogen** use is assocd. with a high risk (relative risk, 2.1 to 5.7) of endometrial hyperplasia and adenocarcinoma, and it has been understood for some time that a progestogen must be added for at least 10 to 14 days per mo to prevent these effects. However, the most commonly used synthetic **progestins**, norethisterone and medroxyprogesterone acetate, have been assocd. with metabolic and vascular side effects (eg, suppression of the vasodilating effect of **estrogens**) in both exptl. and human controlled studies. All comparative studies to date conclude that the side effects of synthetic **progestins** can be minimized or eliminated through the use of natural progesterone, which is identical to the steroid produced by the corpus luteum. The inconvenience assocd. with the use of injectable, rectal, or vaginal formulations of natural progesterone can be circumvented by using orally administered **micronized** progesterone. The bioavailability of **micronized** progesterone is similar to that of other natural steroids, and interindividual and intraindividual variability of area under the curve is similar to that seen with synthetic **progestins**. A clear dose-ranging effect has been demonstrated, and long-term protection of the endometrium has been established. **Micronized** progesterone has been used widely in Europe since 1980 at dosages ranging from 300 mg/d (taken at bedtime) 10 days a month for women wishing regular monthly bleeding to 200 mg 14 days a month or 100 mg 25 days a month for women willing to remain amenorrheic. This therapy is well tolerated, with the only specific side effect being mild and transient drowsiness, an effect minimized by taking the drug at bedtime. The prospective, comparative Postmenopausal **Estrogens/ Progestin** Intervention trial has recommended oral **micronized** progesterone as the first choice for opposing **estrogen** therapy in nonhysterectomized postmenopausal women.

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L4 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:160636 CAPLUS
DOCUMENT NUMBER: 124:251184
TITLE: Effects of hormone replacement therapy on endometrial histology in postmenopausal women. The postmenopausal estrogen/progestin interventions (PEPI) trial
AUTHOR(S): Judd, Howard L.
CORPORATE SOURCE: National Heart, Lung, and Blood Institute, National Institutes Health, Bethesda, MD, 20892-7956, USA
SOURCE: JAMA, J. Am. Med. Assoc. (1996), 275(5), 370-5
CODEN: JAMAAP; ISSN: 0098-7484
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Histol. findings of the endometrium of postmenopausal women who were randomized to receive placebo, **estrogen** only, or one of three **estrogen** plus **progestin** (E+P) regimens in the Postmenopausal **Estrogen/Progestin** Interventions (PEPI) Trial are reported. A 3-yr multicenter, randomized, double-masked, placebo-controlled trial was undertaken. A total of 596 postmenopausal women aged 45 through 64 yr without contraindication to hormone therapy were included. Participants were randomized and stratified in equal nos. to one of the following treatments in 28-day cycles: placebo, 0.625 mg/d of conjugated equine **estrogens** (CEE), 0.625 mg/d of CEE plus 10 mg/d of medroxyprogesterone acetate (MPA) for the first 12 days, 0.625 mg/d of CEE plus 2.5 mg/d of MPA, or 0.625 mg/d of CEE plus 200 mg/d of **micronized** progesterone (MP) for the first 12 days. During follow-up women assigned to **estrogen** alone were more likely to develop simple (cystic), complex (adenomatous), or atypical hyperplasia than those given placebo (27.7% vs. 0.8%, 22.7% vs. 0.8%, and 11.8% vs. 0%, resp.) for the same types of hyperplasia. Participants administered one of the three E+P regimens had similar rates of hyperplasia as those given placebo. The occurrence of hyperplasia was distributed evenly across the 3 yr of the trial. Women taking **estrogens** alone also had more unscheduled biopsies (66.4% vs. 8.4%) and curettages (17.6% vs. 0.8%) than women receiving placebo. The no. of surgical procedures was similar for women receiving placebo and women receiving the E+P regimens. Of the 45 women with complex (adenomatous) or atypical hyperplasia, study medications were discontinued in all, and the biopsy results of 34 (94%) of 36 women with hyperplasia reverted to normal with **progestin** therapy. The remainder had dilatation and curettage (n=2) or hysterectomy with (n=2) or without (n=6) prior medical therapy, or refused further biopsies (n=1). One woman developed adenocarcinoma of the endometrium while receiving placebo. Thus, at a dosage of 0.625 mg, the daily administration of CEE enhanced the development of endometrial hyperplasia. Combining CEE with cyclic or continuous MPA or cyclic MP protected the endometrium from hyperplastic changes assocd. with **estrogen**-only therapy.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:276225 CAPLUS

DOCUMENT NUMBER: 132:284090

TITLE: Improved bioavailability of a micronized megestrol acetate tablet formulation in humans

AUTHOR(S): Farinha, A.; Bica, A.; Tavares, P.

CORPORATE SOURCE: Laboratorio de Estudos Farmaceuticos, Lisbon, 1400, Port.

SOURCE: Drug Development and Industrial Pharmacy (2000), 26(5), 567-570
CODEN: DDIPD8; ISSN: 0363-9045

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Megestrol acetate, a **progestogen** widely used in the palliative treatment of endometrial carcinoma and breast cancer, is currently administered orally as a solid dosage form. **Bioavailability** of the drug following oral administration is closely related to the effectiveness and safety profile of the drug in formulation. Improved immediate-release formulations should allow improved drug delivery into the systemic circulation and, at the end, to the site of action. The micronization of drugs is one of the technol. procedures to achieve such a purpose. This paper reports the design and results obtained in an in vivo study of the **bioavailability** of a **micronized** megestrol acetate tablet formulation compared to a conventional form. A significant increase in the drug **bioavailability** was obsd., in either the rate or the extent of **absorption**. In vitro dissoln. data of the 2 study formulations reflected the in vivo findings.

L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:240410 CAPLUS
DOCUMENT NUMBER: 112:240410
TITLE: **Bioavailability** of composite injection of **norgestrel** with different **particle** size
AUTHOR(S): Zhao, Zhifang; Li, Quan; Chu, Yunhong
CORPORATE SOURCE: Dep. Pharmacol., Shanghai Med. Univ., Shanghai, 200032, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (1989), 20(11), 501-3
CODEN: ZYGZEA; ISSN: 1001-8255
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

TI **Bioavailability** of composite injection of **norgestrel** with different **particle** size

AB The serum concns. of levonorgestrel and estradiol in rabbits following i.m. administration of a composite injection of **norgestrel** with different **particle** sizes (5 or 15 .mu.m) were measured by RIA. Results from pharmacokinetic data indicated that there is no difference in the **bioavailability** of **norgestrel** with different **particle** sizes.

ST **norgestrel** injection **bioavailability particle** size

IT Drug **bioavailability**
(of **norgestrel** composite injections, **particle** size effect on)

IT **Particle** size
(of **norgestrel** in composite injections, **bioavailability** in relation to)

IT 6533-00-2, **Norgestrel**
RL: PROC (Process)
(**bioavailability** of, in composite injections, **particle** size effect on

L7 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:276225 CAPLUS
DOCUMENT NUMBER: 132:284090
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AUTHOR(S): Farinha, A.; Bica, A.; Tavares, P.
CORPORATE SOURCE: Laboratorio de Estudos Farmaceuticos, Lisbon, 1400, Port.
SOURCE: Drug Development and Industrial Pharmacy (2000), 26(5), 567-570
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
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L4 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:442016 CAPLUS
DOCUMENT NUMBER: 115:42016
TITLE: Estrogen and cardiovascular disease
AUTHOR(S): Lobo, Rogerio A.
CORPORATE SOURCE: Sch. Med., Univ. South. California, Los Angeles, CA, 90033, USA
SOURCE: Ann. N. Y. Acad. Sci. (1990), 592(Multidiscip. Perspect. Menopause), 286-94
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 39 refs., of the beneficial effects of natural **estrogens** on cardiovascular function. Types of **estrogen** which have been considered to be natural include conjugated equine **estrogen**, **estradiol** (either **micronized** or as the valerate ester), and estrone sulfate. The beneficial effects of these **estrogens** on the cardiovascular system are summarized by examg. the specific effects of postmenopausal **estrogen** replacement on blood pressure, carbohydrate metab., coagulation, psychol. function, and cardiovascular death rate (epidemiol.). Mechanisms of the cardioprotective effect of **estrogens** are discussed, along with the impact of **progestins**.

L4 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:46434 CAPLUS
DOCUMENT NUMBER: 124:76810
TITLE: Insulin-like growth factor-binding protein-1: a biochemical marker of endometrial response to progestin during hormone replacement therapy
AUTHOR(S): Suvanto-Luukkonen, Eila; Sundstroem, Helena; Penttinen, Jorma; Kauppila, Antti; Rutanen, Eeva-Marja
CORPORATE SOURCE: Dept. Obstetrics and Gynecology, Oulu Univ. Central Hospital, Oulu, 90220, Finland
SOURCE: Maturitas (1995), 22(3), 255-62
CODEN: MATUDK; ISSN: 0378-5122
DOCUMENT TYPE: Journal
LANGUAGE: English

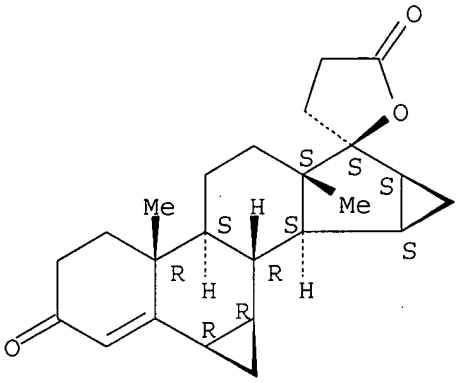
AB Endometrial samples for morphol. examn. and immunohistochem. staining with monoclonal antibody against IGFBP-1 were obtained from 30 menopausal women before treatment and after 12 and 24 mo of continuous combined hormone replacement therapy (HRT). All women received percutaneous **estradiol**-gel releasing 1.5 mg **estradiol** daily. Regarding **progestins**, patients were divided into three groups: one group had a 20 .mu.g/24 h levonorgestrel-releasing intrauterine device (LNG-IUD); the women in the other two groups received **micronized** natural progesterone either 100 mg orally or 100-200 mg vaginally daily, 25 days per calendar month. Before treatment the endometrium of all women was atrophic or subatrophic and no IGFBP-1 could be detected in any of the samples which contained enough stromal cells for evaluation. After 12 and 24 mo of treatment, epithelial atrophy with decidual transformation in stroma was detected in all specimens in the LNG-IUD group, and IGFBP-1 was localized in decidualized stromal cells in all samples. In the other two groups, no signs of **progestin** effect were detected by microscopic examn. in any of the endometrial samples and IGFBP-1 staining was completely neg. in all of them. A striking difference occurred in both morphol. and biochem. response in the endometrium of women treated with LNG-IUD compared with those receiving oral or vaginal **micronized** progesterone during continuous combined HRT. **Micronized** progesterone at doses used in this study turned out to be ineffective to prevent the proliferative effect of **estrogen**. Immunohistochem. localization of IGFBP-1 in endometrial stromal cells strongly correlated with decidual reaction in all endometrial specimens exposed to LNG-IUD, suggesting that the immunostaining of IGFBP-1 can be used as a means of assessing the strength of **progestin** effect in the endometrium during HRT.

L4 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:305604 CAPLUS
DOCUMENT NUMBER: 127:29238
TITLE: Effect of postmenopausal hormone therapy on body weight and waist and hip girths
AUTHOR(S): Espeland, Mark A.; Stefanick, Marcia L.; Kritz-Silverstein, Donna; Fineberg, S. Edwin; Maclawiw, Myron A.; James, Margaret K.; Greendale, Gail A.
CORPORATE SOURCE: Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, NC, 27157, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (1997), 82(5), 1549-1556
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reports from cross-sectional comparisons, nonrandomized prospective studies, and relatively small clin. trials indicate that postmenopausal hormone therapy may slightly decrease the amt. of wt. typically gained by women during the decade following menopause. Despite this, widespread belief remains that hormone therapy may cause wt. gain. The authors use data from the Postmenopausal **Estrogen/Progestin** Interventions trial to characterize the impact of postmenopausal hormone therapy on wt. and fat distribution and to examine the consistency of this impact among subgroups of women defined by lifestyle, clin., and demog. factors. The Postmenopausal **Estrogen/Progestin** Interventions trial was a 3-yr, placebo-controlled, randomized clin. trial of 875 women assessing the effects on cardiovascular risk factors of four hormone regimens: oral conjugated equine **estrogen** (CEE) therapy (0.625 mg daily alone), CEE in combination with medroxyprogesterone acetate (2.5 mg daily), CEE in combination with medroxyprogesterone acetate (10 mg daily on days 1-12), and CEE in combination with **micronized** progesterone (200 mg daily on days 1-12). Women randomly assigned to CEE with or without a progestational agent averaged 1.0 kg less wt. gain at the end of 3 yr than those assigned to placebo. Assignment to CEE was also assocd. with avs. of 1.2 cm less increase in waist girth and 0.3 cm less increase in hip girth. In regression models that included wt. change as a covariate, none of these differences reached statistical significance. There were no significant differences in wt. or girth changes among any of the four active hormone regimens. After accounting for the effects of assignment to active hormone therapy and baseline wt., older age and higher phys. activity level at baseline were also independently predictive of less wt. gain. The impact of hormone therapy on wt. gain was similar among subgroups, except for those defined by baseline smoking status and phys. activity level at home. Factors that were independently assocd. with smaller increases in girths were: for waist, greater overall activity and Hispanic ethnicity; and for hip, work activity and greater alc. consumption. None of these factors significantly affected the obsd. overall relationships between **estrogen** and changes in girth.

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 67392-87-4 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, (2'S,6R,7R,8R,9S,10R,13S,14S,15S,16S)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, [6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.alpha.,16.alpha.,17.beta.)]-
OTHER NAMES:
CN 1,2-Dihydrospirorenone
CN 3-Oxo-6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-17.alpha.-pregn-4-en-21,17-carbolactone
CN Dihydrospirorenone
CN **Drospirenone**
CN ZK 30595
FS STEREOSEARCH
MF C24 H30 O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMLIST, CIN, DDFU, DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



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99 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
99 REFERENCES IN FILE CAPLUS (1957 TO DATE)